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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,395	06/08/2001	David K. Gardner	033948-0102	7684

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EXAMINER	
ANGELL, JON E	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 11/20/2002

12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/877,395	GARDNER ET AL.	
	Examiner	Art Unit	
	J. Eric Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) *21-25 and 34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20 and 26-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☒ Interview Summary (PTO-413) Paper No(s). *11* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Action is in response to the Amendment filed on 8/29/02 as Paper No. 10. The amendment has been entered. Claims 6, 10, 17, 26, 30 and 33 have been amended. Claims 1-34 are pending in the application. Claims 21-25 and 34 are drawn to a non-elected invention and have been withdrawn from consideration, as set forth in the previous Office Action (mailed 5/23/02; Paper No. 8).

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 6, 10-20 and 26-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 6, 10, 17, 26, 30 and 33 recite the phrase "capable of". This phrase renders the claims indefinite because it is unclear if the media actually does increase the viability of gametes or embryonic cells cultured in the medium or if the media is merely capable of increasing viability of the cells, but does not actually increase viability. The dependent claims incorporate all of the limitations of the independent claim from which it depends, therefore the dependent claims are rejected for the same reason.

Claim Rejections - 35 USC § 103

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-6, 10-20 and 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skelnick (U.S. Patent 6,153,582) in view of Becquart (U.S. Patent 5,612,196) and Kjems (Acta Pat. Microbiol. Scand. Sect. B 84:162-164, 1976).

Skelnick teaches a defined serum-free composition comprising a glycosaminoglycan, such as hyaluronic acid, in the range of .001mg/ml to 1.0g/ml; a deturgescent agent, such as albumin, in the range of .001mg/ml to 1.0g/ml; and a buffer system, such as sodium citrate, in a range of .01mM to 10mM (see col. 3, lines 52-67) in a medium that can support cell development, here MEM, TC199, or HTF (see col. 3, lines 49-51). Skelnick also teaches that non-human derived serum contains many substances capable of eliciting an immune response (see col. 3, lines 2-3).

Skelnick does not explicitly teach that that the albumin used is recombinant human albumin.

Skelnick also does not teach that the Hyaluronic Acid (HA) is fermented Hyaluronin (fHA)

Becquart teaches a recombinant human albumin which posses all of the properties of human albumin extracted from sera (see col.3, lines 11-14). Becquart teaches that recombinantly producing human albumin removes the risk of viral contamination (see col. 1, lines 53-57) and greatly lowers the risk of immunogenic reactions when used in pharmaceutical applications (see col. 3, lines 47-49).

Kjems teaches a method for producing fermented Hyaluronic Acid using cultures of Streptococci (see all of p. 162). Kjems teaches,

> "The use of chemically defined medium for the preparation of hyaluronic acid ensures reproducibility in yield and degree of purity of the hyaluronic acid. Complications associated with the fact that an undefined substrate contains substances of high molecular weight, e.g. protein, are avoided." (p. 164)

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the media taught by Skelnick by substituting recombinant human albumin for albumin and substituting fermented hyaluronic acid for hyaluronic acid, thus creating a supplement that was free of non-recombinant human albumin and hyaluronan derived from warm blooded vertebrates, with a reasonable expectation for success. The motivation to substitute fermented hyaluronic acid would have been to make a media comprising pure hyaluronic acid in order to avoid complications associated with the use of hyaluronic acid contaminated with high molecular weight substances such as proteins (suggested by Kjems, p. 164). The motivation to substitute recombinant human serum albumin would have been to make a serum-free media free of non-human serum (such as albumin, a serum protein; suggested by Skelnick), to reduce the probability of inducing an immune response (which is possible when the corneal cells are transplanted; suggested by Skelnick: col. 3, lines 2-4, and Becquart: col. 3, lines 47-49), and to reduce the risk of viral contamination (suggested by Becquart: col. 1, lines 55-57). It is noted that replacing the albumin with recombinant human albumin in the defined serum-free media of Skelnick, would produce a medium that is free of non-recombinant human albumin.

2. Claims 1-20 and 30-33 rejected under 35 U.S.C. 103(a) as being unpatentable over Ellington et al. (US Patent 6,140,121) in view of Becquart (U.S. Patent 5,612,196) and Kjems

(Acta Pat. Microbiol. Scand. Sect. B 84:162-164, 1976) and further in view of Skelnick (U.S. Patent 6,153,582).

Ellington teaches a medium such as Ham's F-10, Earl's, Whitten's or PBS for culturing sperm, embryos, or embryonic stem cells (see col. 16, 13-19) comprising a macromolecule, a buffer, as well as a protein (see col. 16, lines 25-35). Ellington teaches that the macromolecule can be hyaluronic acid (see col. 13, lines 56-65), the buffer can be sodium citrate (see col. 16, line 57), and the protein can be human albumin (see col. 16, lines 25-35; and col. 13, lines 56-65).

Ellington does not teach that the media comprises fermented hyaluronic acid.

Ellington does not teach that the media comprised recombinant human albumin.

Ellington does not teach that the media comprises citrate in the range of about 0.1mM to about 1.0mM.

Skelnick teaches a defined serum-free composition comprising a glycosaminoglycan, such as hyaluronic acid, in the range of .001mg/ml to 1.0g/ml; a deturgescent agent, such as albumin, in the range of .001mg/ml to 1.0g/ml; and a buffer system, such as sodium citrate, in a range of .01mM to 10mM (see col. 3, lines 52-67) in a medium that can support cell development, here MEM, TC199, or HTF (see col. 3, lines 49-51). Skelnick also teaches that non-human derived serum contains many substances capable of eliciting an immune response (see col. 3, lines 2-3).

Skelnick does not explicitly teach that that the albumin used is recombinant human albumin.

Skelnick also does not teach that the Hyaluronic Acid (HA) is fermented Hyaluronin (fHA)

Becquart teaches a recombinant human albumin which posses all of the properties of human albumin extracted from sera (see col.3, lines 11-14). Becquart teaches that recombinantly producing human albumin removes the risk of viral contamination (see col. 1, lines 53-57) and greatly lowers the risk of immunogenic reactions when used in pharmaceutical applications (see col. 3, lines 47-49).

Kjems teaches a method for producing fermented Hyaluronic Acid using cultures of Streptococci (see all of p. 162). Kjems teaches,

> "The use of chemically defined medium for the preparation of hyaluronic acid ensures reproducibility in yield and degree of purity of the hyaluronic acid. Complications associated with the fact that an undefined substrate contains substances of high molecular weight, e.g. protein, are avoided." (p. 164)

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the media taught by Ellington by substituting recombinant human albumin for albumin and substituting fermented hyaluronic acid for hyaluronic acid, thus creating a supplement that was free of non-recombinant human albumin and hyaluronan derived from warm blooded vertebrates, with a reasonable expectation for success. The motivation to substitute fermented hyaluronic acid would have been to make a media comprising pure hyaluronic acid in order to avoid complications associated with the use of hyaluronic acid contaminated with high molecular weight substances such as proteins (suggested by Kjems, p. 164). The motivation to substitute recombinant human serum albumin would have been to make a serum-free media free of non-human serum (such as albumin, a serum protein; suggested by Skelnick), to reduce the probability of inducing an immune response (which is

possible when the corneal cells are transplanted; suggested by Skelnick: col. 3, lines 2-4, and Becquart: col. 3, lines 47-49), and to reduce the risk of viral contamination (suggested by Becquart: col. 1, lines 55-57). It is noted that replacing the albumin with recombinant human albumin in the defined serum-free media of Skelnick, would produce a medium that is free of non-recombinant human albumin.

Furthermore, It would have been prima facie obvious to perform routine optimization to optimize the concentrations of the fermented hyaluronic acid, recombinant human albumin, and citrate in the media based on the teachings of Skelnick, as noted in *In re Aller*, 105 USPQ 233 at 235,

> "More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Routine optimization is not considered inventive and no evidence has been presented that the specific concentrations of the reagents used in the media was other than routine optimization, that the product resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

3. Claims 26-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Skelnick (U.S. Patent 6,153,582) in view of Becquart (U.S. Patent 5,612,196) and Kjems (Acta Pat. Microbiol. Scand. Sect. B 84:162-164, 1976), and further in view of Stratagene (Catalog, p. 39, 1998).

Skelnick, Becquart and Kjems teach a media comprising fermented hyaluronic acid, recombinant human albumin and citrate, as mentioned above.

Skelnick does not teach that the reagents used to make the media are in a kit for supplementing culture medium wherein the kit comprises the reagents used to make the media (mammalian culture media, recombinant human albumin, fermented hyaluronin, and citrate and free of non-recombinant human albumin and/or fermented hyaluronin) and instructions on how to use the kit to make a culture media, comprising the mentioned reagents at the appropriate concentrations.

However, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the reagents required for making the medium composition suggested by Skelnick, Bacquart and Kjems (as mentioned above) into a kit format with instructions as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents into a kit. Specifically, the Stratagene catalog teaches "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

Claim Rejections - 35 USC § 112

Response to Arguments

4. The rejection of claims under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention are withdrawn. However, new rejections under 35 USC 112, second paragraph are necessitated by the claim amendments.

Claim Rejections - 35 USC § 102

Response to Arguments

5. Applicant's arguments with respect to the claims rejected under 35 U.S.C. 102(b) have been considered and are persuasive with respect to the failure of the cited references to teach a culture media comprising fermented hyaluronic acid, and recombinant human albumin. The rejection of claims under 35 USC 102(b) are withdrawn.

Claim Rejections - 35 USC § 103

Response to Arguments

6. Applicant's arguments with respect to the claims rejected under 35 USC 103 have been considered but are moot in view of the new ground(s) of rejection.

Applicants argument that the cited references do not teach a composition comprising ferreted hyaluronin are persuasive. The new rejections incorporate a reference to address the substitution of fermented hyaluronin for non-fermented hyaluronin taught by the cited references.

7. With respect to Applicants argument that there is no suggestion in the cited references that the media would be capable of increasing the viability of gametes or embryonic cells as mentioned in the claims, first it is pointed out that the phrase "capable of" does not limit the claims to a media that does actually increase viability, but also encompasses the media that does not actually increase viability (see the rejection under 35 USC 112, second paragraph above). Furthermore, increasing the viability of gametes or embryos is considered to be an intended use for the media. It is respectfully pointed out that a recitation of the intended use of the claimed invention (here, the culture media/supplement) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Without a clear indication that the claimed media is structurally different from the media made by combining the cited references, both media would be capable of performing the intended use (increasing viability). Furthermore, in order to overcome the rejection by a Declaration indicating unexpected results, the Declaration must include data indicating that the media comprising fermented hyaluronin and recombinant human

albumin would confer a greater viability to gametes and embryonic cells than the media with non-fermented hyaluronin and non-recombinant human albumin.

In response to Applicants argument that claims 30 and 33 recite the phrase, "consisting essentially of" and thus limit the claims to only the elements specifically listed and other ingredients that do not interfere with or contribute to the activity of the composition. It is respectfully pointed out that the phrase "consisting essentially of" is not closed language limiting the claims to only the specifically listed elements, but is open language allowing other elements as well as those listed.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell
November 12, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER